

DRAFT

EXAMINER'S AMENDMENT

Note re: claim 67: You and your client may amend this claim further. The idea here is that a pump (a pressure control device) is connected to the microchannel for pumping fluid in both directions, in and out of the microchannel, to pump fluid into and out of the measurement chamber. Maybe fluid is pumped only in one direction, depending on what you want to claim. As long as the idea is clear, the exact wording of the claim is flexible.

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Applicants' representative, Mr. Andrew Shyjan, on August ??, 2011.

The application has been amended as follows.

The claims have been amended as follows. Claims 55, 60, 64, 65, 67, 71, 83, 91 and 104 have been amended as shown below. Claims 1-54, 56-59, 61-63, 66, 68-70, 72-82, 84-90, 92-103, 105 and 106 remain as shown in the amendment filed on July 29, 2011. Of these claims, claims 1-54, 63, 66, 68-70, 72-82, 84-88, 90, 92-103 and 106 have been canceled.

55. (currently amended) A microfluidic system comprising:

- a) at least one measurement chamber wherein the measurement chamber comprises walls and a base;
- b) at least one hollow nanotip protruding from the walls or base of the measurement chamber and having an aper[[a]]ture at an end of the nanotip;[[::]] and
- c) at least one microchannel connected to ~~in communication with~~ the measurement chamber, the microchannel having at least one inlet positioned to receive an aqueous

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solution and at least one outlet positioned to deliver the aqueous solution into the measurement chamber.

60. (currently amended) A microfluidic system comprising:

- a) at least one measurement chamber comprising walls and a base;
- b) a plurality of electrode tips wherein the electrode tips protrude from the walls or base of the measurement chamber; and
- c) at least one microchannel connected to ~~in communication with~~ the measurement chamber, wherein the microchannel comprises at least one inlet positioned to receive an aqueous solution and at least one outlet positioned to deliver the aqueous solution into the measurement chamber.

64. (currently amended) The system of claim 62, wherein the at least one contacting surface has ~~comprises~~ a diameter of less than ~~about~~ 5 μm .

65. (currently amended) The system of claim 62, wherein the at least one contacting surface has ~~comprises~~ a diameter of less than ~~about~~ 1 μm .

67. (currently amended) The system of claim 55 or 60, further comprising a pressure control device connected to the ~~at least one~~ microchannel, for controlling positive and negative fluid pressure applied to ~~in the~~ at least one microchannel, for pumping fluid in and out of the microchannel.

71. (currently amended) The system of claim 55 or 60, wherein the microchannel in the microfluidic system is connected interfaced to a multiwell plate through one or more external tubings or capillaries.

83. (currently amended) The system of claim 55 or 60, further comprising an amplifier
connected to in communication with the at least one nanotip or electrode.

The following is an examiner's statement of reasons for allowance. The claims are free of the prior art. As discussed in the previous Office actions, Maher et al. (US 2002/0025568 A1) disclose an apparatus for carrying out electrical measurements on cells. The apparatus comprises a substrate comprising an array of measurement chambers (a microtiter plate) that contain cells. The measurement chambers have walls surrounding a base. The apparatus comprises an array of microelectrodes that match the wells in the microtiter plate and that are arranged in a lid or cover. The electrodes may be solid (i.e., have solid tips) or fluid filled (patch clamp electrodes). Patch clamp electrodes have a tip, a housing that defines a lumen and an aperture, and they can be inserted into a cell membrane, which is a lipid-based cell structure. The tip has a contacting surface that has a diameter of about one micron. The electrode is filled with a conducting electrolyte solution (a buffered salt solution). See Figs. 1, 3 and 9 and paragraphs 11, 15, 127, 136, 137, 143, 144 and 160. Hamill et al. ("Improved patch-clamp techniques for high-resolution current recording from cells and cell-free membrane patches," Pflügers Archiv 391:85-100, 1981) provide further disclosure on the structure and use of patch clamp electrodes (see p. 86, second full paragraph and right col.; p. 91, left col.; p. 92, left col.; and Figs. 1, 2A, 6A, 9 and 10 on pp. 86, 87, 91, 93 and 94). The apparatus is part of a computer-controlled system that operates the electrical, mechanical and optical aspects of the apparatus, as it controls the activity of the electrodes, movement of the microtiter plate, spectroscopic readings of the wells in the microtiter plate, and data collection and analysis. The electrodes are compatible with microfluidics equipment (see paragraphs 197, 198, 202 and 205-208). Maher et al. do not disclose that the measurement chambers have microchannels.

He et al. (US 2003/0049862 A1) disclose a microfluidics system, in which the

microfluidics plumbing is incorporated into the lid for a standard microtiter plate, thereby providing the measurement chambers with microchannels that are inlets and outlets. The outlets can deliver an aqueous solution to the measurement chambers from a reservoir of that fluid (continuous fluid delivery). See paragraphs 6-12 and 35-45. The measurement chambers are circular and the microchannels may be radially disposed with outlets in the chambers (see paragraph 39). The system comprises a pressure control device for controlling the positive and negative fluid pressures to the microchannels, which fill and empty the measurement chambers, allowing assays to be performed and the chambers to be washed (see paragraph 49).

The claimed microfluidics system no longer reads on the apparatus of Maher et al. in which the microtiter plate lid has been modified with the microfluidics plumbing of He et al. The claims now recite that the electrically conductive nanotip or electrode tip protrudes from the base or the walls of the measurement chamber, not from the lid. Altering the apparatus of Maher et al., in which the microtiter plate lid is modified with the plumbing of He et al., so that the electrodes/nanotips protrude from the base or the walls instead of from the interior of the lid is not a change that is suggested by the cited art. This change is not suggested, because the apparatus of Maher et al. and He et al. are designed to be compatible with standard microtiter plates. Thus, in the apparatus in the prior art, the electrodes/nanotips must be part of the lid (which is removable for cleaning and loading), not part of the plate.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROSANNE KOSSON whose telephone number is (571)272-2923. The examiner can normally be reached on Mon., Thurs., Fri., 8:30-6:00, Tues., 8:30-2:00, Wed. off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Rosanne Kosson/
Primary Examiner, Art Unit 1657
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